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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MITRA, RITA

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application N .	Applicant(s)	
	09/105,117	VRLIJC ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-20,43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10-20, 43 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Applicants' amendment and response to office action dated May 21, 2002, filed on July 19, 2002 in paper #40 is acknowledged. Claims 1, 4, 7, 8, 10, 12-20, 43 and 46-48 have been amended and entered. Claims 9, 44 and 45 have been cancelled. Therefore, claims 1-8, 10-20, 43 and 46-48 are currently pending to which the following grounds for rejection are or remain applicable.

Objection to claims

Claims 1, 8, 16, 18 and 19 objected to because of the following informalities:

Claims 1, 8, 16, 18 and 19 are indefinite because of extraneous periods (see "SEQ ID NO."), which should be "SEQ ID NO:". Claims 2-7, 10-15, 17 and 20 are included in this objection because they depend on objected base claims.

Appropriate correction is required.

Response to Remarks and Arguments

Rejection under 112, second paragraph

The previous rejection of claims 1-20 and 43-48 under **35 U.S.C. 112, second paragraph**, being indefinite is withdrawn in view of applicants' amendment to the claims.

Rejection under 35 U.S.C. 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 and dependent claims 2-20 stand/are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a process for microbacterial production of amino acids by providing a microbial organism having a certain export carrier activity and a certain export gene expression, wherein the export gene amino acid sequence is set forth in SEQ ID NO: 2 and a regulatory protein sequence is set forth in SEQ ID NO: 3; does not reasonably provide enablement for a process using mutation of export carrier gene and regulatory proteins of SEQ ID NO: 2 and SEQ ID NO: 3 respectively. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 and the dependent claims 2-8 and 10-20 thereto are directed to a process for the microbial production of amino acids using a gene construct, having an export gene that encodes an amino acid sequence of SEQ ID NO: 2, wherein the regulatory gene of the construct encodes an amino acid sequence as set forth in SEQ ID NO: 3. Claim 1 also encompasses an increased production of amino acids in accordance with export gene expression endogenous to said microbial organism by selecting a step of mutating the export carrier gene such that an export carrier with increased export activity is generated. The specification, however, only discloses cursory conclusions (see page 6), without data to support the findings, which state that in general a functional derivative that can be obtained by deletion, insertion and/or substitution, wherein the regulator protein activity or function is retained or even increased, however the specification fails to provide a specific description or a demonstration of any mutant of export carrier gene and/or regulator gene that retains the activity of wild type. There are no indicia that the present application enables the full scope in view of the amino acid sequences corresponding to an export gene and a regulatory gene products as set forth in SEQ ID NO: 2 and SEQ ID NO: 3 or a mutant thereof as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims 3) the amount of direction or guidance presented; 4) the presence or absence of working

examples; 5) the quantity of experimentation necessary; 5); 6) the predictability or unpredictability of the art; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) the nature of the invention:

The nature of the invention is defined by the claims, which include a process for the microbacterial production of amino acids by providing a microbial organism using a gene construct, having an export gene that encodes an amino acid sequence of SEQ ID NO: 2, wherein the regulatory gene of the construct encodes an amino acid sequence as set forth in SEQ ID NO: 3 and the mutants thereof. However the specification does not provide the information on the structure and function of the claimed mutants.

2) the breadth of the claims:

The breadth of the claims is broad and encompasses an unspecified number of variants regarding the export gene protein of SEQ ID NO: 2 and a regulatory protein of SEQ ID NO: 3 as biological active fragments, which are not specifically described or demonstrated in the specification. The specification describes at page 6 as "allelic variations or, respectively, equally effective DNA sequences comprise particularly functional derivatives which can be obtained by deletions, insertion or substitution of nucleotides of corresponding sequences..." However the specification at page 6, lines 7-19 describes a functional derivative that can be obtained by mutation but it does not provide a definition of a mutant. The specification does not describe what might be considered a mutant of the DNA of claims 3, 5, 7, 8, 10, 15, 17, 18 and 20 or provide any examples of the same. It does not appear that mutants have been generated or identified.

As for factors 3-5:

3) the amount of direction or guidance presented;

4) the presence or absence of working examples; and

5) the quantity of experimentation necessary:

The specification at page 6 provides a generic description for obtaining variants by deletion, insertion and/or substitution of nucleotides of corresponding sequences, wherein however the regulator protein activity or function is retained or even increased. Furthermore, the specification describes and demonstrates the production and increased accumulation of L-lysine by export gene (LysE) and regulator gene (LysG) in Examples e) and f) at page 13-14, however no description or Examples are provided for the enablement of claimed variants. The experimentation involved to enable the invention may constitute routine experimentation, however, because of the limited information in the specification it would require undue and excessive experimentation. No specific description is provided about the position of the corresponding sequence of SEQ ID NO: 2 and SEQ ID NO: 3 where amino acid substitution is suggested neither any activity of those variants have been demonstrated. Without more guidance from the specification it would require an undue and excessive experimentation for a person having skill in the art to be able to make and use the claimed analogs.

6) the predictability or unpredictability of the art:

The invention is highly unpredictable for the reasons set forth for factors 1-5.

As for factors 7 and 8:

7) the state of the prior art

8) the relative skill of those skilled in the art:

The prior art has shown that the flux of L-lysine biosynthesis in wild-type *Corynebacterium glutamicum* is increased by L-methionine addition (see Vrljic et al. J. of Bacteriology, vol 177 (4), July 1995), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structure and function for allelic variants.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because in summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable for the various modified forms, it is necessary to have additional guidance and to

carry out further experimentation to assess the property of the variants. Therefore, due to large quantity of experimentation necessary to determine an activity or property of the disclosed process using export gene and the variants thereof, such that it can be determined how to use the claimed process, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the specification fails to teach the skilled artisan how to make and use the claimed invention.

Applicants' comments regarding "allele variation" at page 8 of the response filed on July 19, 2002 is noted and this part of the objection has been withdrawn in light of applicants' amendments to the claims, however applicants fail to address the objection regarding "mutant variants" raised in the previous office action. The specification fails to provide any description of the claimed mutants with the same function as the wild type gene. Therefore, as the specification fails to describe adequately the structure and function of those mutants, one skilled in the art would not recognize a specific utility for those variants and would not know how to use them. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed variants.

Rejection under 35 U.S.C. 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is also indefinite because steps i)- iv) are missing. A correction in numbering the steps would overcome the rejection.

Claim 1 is also indefinite because amended claim still lacks some essential steps as claimed in the process for the microbacterial production of amino acids. The omitted steps are: insertion of the construct into a suitable vehicle and transformation of a suitable host cell,

culturing the transformed cells and recovering the amino acids from the culture, and a step whereby the desired outcome can be determined.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 43, 46-48 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). The amended claim 43 has included the steps, however the claim still recites "use." An amendment "A process for the microbial production of amino acids using export gene may overcome this rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
May 15, 2003

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